

## REMARKS

### 1. Claim Amendment

Claims 53-55, 62, 64, 66, 67, 72, and 73 have been amended to correct obvious typographic errors and in response to the Examiner's comments regarding compliance with section 112, second paragraph.

The dependency of claim 62 has been corrected as suggested by the Examiner. The change in dependency provides proper antecedent basis for the recitations in claim 62. The scope of this claim is not changed by the amendment.

Claim 64 has been made dependent from claim 63 in response to the restriction requirement so that claims 63 and 64 would be placed in the same group for election. Applicants reserve their right to pursue the subject matter of original claim 64 in a division, if necessary.

Claims 53-55, 66, 67, 72, and 73 have been amended to replace the term "protective group" with "protective group reagent." The term protective group reagent is found on page 25, line 3 where the context of its usage indicates that it is a reagent for adding protective groups to the peptides. The Examiner indicated that the term "protective group" did not refer to a compound, but to a portion of a compound. It is believed that the amendment corrects this error in usage. Applicants believe however that the term linker as employed in the specification refers to a compound. The term linker refers on as stated in the specification at page 7, lines 10-14 to a species "carrying a reactive group or a latent reactive group that will facilitate selective attachment of phosphoproteins or phosphopeptides to a label or to a solid surface." In contrast, the term "linker group" refers more correctly to the group that remains after reaction of the linker. It is believed that the claims as amended are clear and definite.

None of the amendments represents the addition of new matter.

## 2. Restriction and Election

The Office has required restriction of the claims in this case into six groups. Applicants elect prosecution of the claims of Group I (claims 1-52 and 68-71) directed to methods of selectively labeling phosphate groups and methods for detecting phosphopeptides. This election is made with traverse and Applicant respectfully requests reconsideration of the imposition of the restriction requirement.

The method claims are combined in a single Group I (the elected group) and the kit claims are subdivided into five groups.

The Office supports restriction between the method and kit claims (Claims of Group I and all other Groups) by stating that “the combination of reagents which define the kit of claim 53 could be used to prepare a wide variety of compounds” and are “not limited to use in preparing the labeled phosphopeptides of Invention I.” The Office characterizes Group VI kits (claim 67) as “useful solely in a method for detecting phosphopeptides.” Thus, the argument given by the Office in support of the restriction of the method and kit claims does not appear to apply at least to the Group VI kit claims. Applicant therefore respectfully requests rejoinder of the claims of Group I and VI.

The Office indicates that claim 53 is directed to “kits comprised of ethanolamine, trifluoroacetic acid and optional amine protective groups.” The language of the claim is however generically directed to a combination of a selected protective group which reacts with both a carboxylic acid or ester and a phosphate group and a mild reagent for selective regeneration of free phosphate groups. This generic recitation of elements is directed to elements useful for the recited purpose of the kit for selective labeling of phosphopeptides. This particular combination is novel and non-obvious for the recited kit application. Thus, Applicants submit that the kit as claimed is directed to a kit for performing selective labeling as claimed in the claims of Group I. Applicants submit that the kit claims and method claims should thus not be restricted. Further a search of all of

the claims of the various method and kit claims will not represent an undue burden on the office.


Finally, claim 64 has been amended to depend from claim 63. It is believed that amended claim 64 should be combined with the kit claims of Group II.

3. Conclusion

Claims 1-73 remain in this case. Applicants have elected prosecution of the claims of Group I (claims 1-52 and 68-71) with traverse.

This amendment and response does not require the payment of any additional fees for excess claims. This amendment is accompanied by a Petition for Extension of Time of Five (5) months with appropriate fee. If the fee submitted is incorrect, please deduct any deficiency or credit any overpayment to deposit account 07-1969.

Respectfully submitted,

  
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53. (once amended). A kit for selectively labeling phosphopeptides in a mixture of peptides which comprises:
- (a) a protective group reagent which reacts with a carboxylic acid or ester thereof and which also reacts with a phosphate group; and
  - (b) a mild acid reagent for selectively regenerating any free phosphate groups in the peptide by reacting the protected peptides under sufficiently mild acid conditions such that the phosphoramidate bond is substantially cleaved and the amide bond is substantially not cleaved.
54. (once amended). The kit of claim 53 wherein the protective group reagent is an amine.
55. (once amended). The kit of claim 53 wherein the protective group reagent comprises differentially isotopically labeled protective groups.
56. The kit of claim 53 further comprising a radiolabel, a fluorescent label, a colorimetric label or an affinity label.
62. (once amended). The kit of claim [53] 56 wherein the label carries a reactive group that can form a covalent bond to a solid phase material and wherein the selectively labeled peptides are separated by first covalently attaching the labeled peptides to the solid phase material, then washing the solid support to remove peptides that are not covalently attached to the support and thereafter releasing peptides from the solid phase material.

64. (twice amended). The kit of claim [53] 63 further comprising a reagent for removing covalently linked phosphopeptides from a solid support.
66. (twice amended). The kit of claim 53 which comprises:
- one or more enzymes for carrying out a peptide digest;
  - one or more protective [groups] group reagents that react with carboxylic acid or carboxylic acid ester groups and with a phosphate group;
  - one or more protective [groups] group reagents that react with the amine groups in the peptides;
  - one or more reagents for selectively cleaving a phosphoramidate bond in the presence of amide bonds to generate free phosphates; and
  - one or more labels which carry a functional group for selectively reacting with free phosphate groups.
67. (twice amended). The kit of claim 53 which comprises:
- one or more enzymes for carrying out a peptide digest;
  - one or more protective [groups] group reagents that reacts with the amine groups in the peptides;
  - one or more protective [groups] group reagents that react with carboxylic acid or carboxylic acid ester groups and with a phosphate group;
  - one or more reagents for selectively cleaving a phosphoramidate bond in the presence of amide bonds to generate free phosphates; and
  - one or more linkers which carry a functional group for selectively reacting with free phosphate groups and carry a reactive group or a latent reactive group for reacting with a solid support material;
  - one or more solid support materials to which the reactive group or the latent reactive group can be attached; and

one or more reagents for cleaving a phosphopeptide from a solid support material.

72. (once amended). The kit of claim 53 further comprising one or more protective [groups] group reagents that react with the amine groups in the peptides.
73. (once amended). The kit of claim 72 wherein the protective [groups ] group of the protective reagent is [are] t-boc or f-moc.--